# Drug-eluting versus bare-metal stent for treatment of saphenous vein grafts: a meta-analysis.

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Abstract: BACKGROUND: Saphenous vein grafts develop an aggressive atherosclerotic process and the efficacy of drug eluting stents (DES) in treating saphenous vein graft (SVG) lesions has not been convincingly demonstrated. The aim of this study was to review and analyze the current literature for controlled studies comparing DES versus bare metal stents (BMS) for treatment of SVG stenoses. METHODOLOGY/PRINCIPAL FINDINGS: We searched several scientific databases and conference proceedings up to March 15, 2010 for controlled studies comparing target vessel revascularization (TVR) between DES and BMS. Summary odds ratios (OR) for the primary endpoint TVR and secondary endpoints infarction, stent thrombosis and death were calculated using random-effect models. A total of 29 studies (3 randomized controlled trials RCT) involving 7549 (202 in RCT) patients were included. The need for target vessel revascularization in the DES group tended to be lower compared to BMS for the 3 RCT (OR 0.50 [0.24-1.00]; p = 0.051) and for observational studies (0.62 [0.49-0.79]; p<0.001). There was no significant difference in the risk for myocardial infarction in the RCT (OR 1.25 [0.22-6.99]; p = 0.250) but a lower risk for DES based on the observational studies 0.68 [0.49-0.95]; p = 0.023. The risk for stent thrombosis was found to be non-different in the RCT (OR 0.78 [0.03-21.73], p = 0.885) while it was in favor of DES in the observational studies (0.58 [0.38 - 0.84]; p<0.001). The mortality was not significantly different between DES and BMS in the RCT's (OR 2.22 [0.17 - 29.50]; p = 0.546) while the observation studies showed a decreased mortality in the DES group (0.69 [0.55-0.85]; p<0.001). CONCLUSION: DES may decrease TVR rate in treatment of SVG stenoses. No differences in reinfarction rate, stent thrombosis or mortality was found between the DES and BMS groups in the RCT's while the observational data showed lower risk for myocardial infarction, stent thrombosis and death in the DES group. This may be a result of patient selection bias in the observational studies or represent a true finding that was not the detected in the RCT analysis due to limited statistical power.

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# Drug-eluting versus bare-metal stent for treatment of saphenous vein grafts: a meta-analysis

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**ABSTRACT**

**Objectives:** The aim of this study was to review and analyze the current literature for controlled studies comparing drug-eluting stents (DES) versus bare-metal stents (BMS) for treatment of saphenous vein graft (SVG) stenoses.

**Background:** Saphenous vein grafts develop an aggressive atherosclerotic process and the efficacy of DES in treating SVG lesions has not been convincingly demonstrated.

**Methods**: We searched several scientific databases and conference proceedings up to February 11, 2010 for controlled studies comparing target vessel revascularization (TVR) between DES and BMS. Summary odds ratios (OR) for the primary endpoint TVR and secondary endpoints infarction, stent thrombosis and death were calculated using random-effect models.

**Results:** A total of 24 studies (3 randomized controlled trials RCT) involving 6391 (202 in RCT) patients were included. The need for target vessel revascularization in the DES group was lower compared to BMS for the 3 RCT (OR 0.51 [0.27 - 0.96]; p=0.037) and for observational studies (0.64 [0.48 - 0.85]; p=0.002). There was no significant difference in the risk for myocardial infarction in the RCT (OR 1.25 [0.22 - 6.99]; p=0.250) nor in the observational studies (0.75 [0.53 - 1.06]; p= 0.107). The risk for stent thrombosis was found to be non-different in the RCT (OR 0.78 [0.03 - 21.73], p=0.885) while it was in favor of DES in the observational studies (0.49 [0.25 - 0.94]; p=0.0324). The mortality was not significantly different between DES and BMS in the RCT's (OR 2.2 [0.17 – 29.5]; p=0.546) while the observation studies showed a decreased mortality in the DES group (OR 0.66 [0.54 - 0.81]; p < 0.0001).

**Conclusion:** DES decrease TVR rate in treatment of SVG stenosis. No differences in reinfarction rate, stent thrombosis or mortality was found between the DES and BMS groups in the RCT's while the observational data showed lower risk for stent thrombosis and death in the DES group which may be a result of selection bias.

Key words: saphenous vein graft, SVG, BMS, DES, meta-analysis.

| **Abbreviations and Acronyms** | |
|---|---|
| BMS | = bare metal stent(s) |
| CABG | = coronary artery bypass graft |
| CAD | = coronary artery disease |
| DES | = drug eluting stent(s) |
| PCI | = percutaneous coronary intervention |
| RCT | = randomized controlled trial(s) |
| ST | = stent thrombosis |
| SVG | = saphenous vein graft |
| MI | = myocardial infarction |
| TVR | = target vessel revascularization |

**Condensed Abstract**

Interventions in saphenous vein grafts (SVG) accounts for about 15% of all percutaneous coronary interventions and the number of such procedures is likely to increase in the future. Little is known about the benefit and risk of drug-eluting stent (DES) in this setting; DES have not been specifically approved for SVG in the U.S. but are used increasingly in an "off-label" fashion. Our meta-analysis of 3 randomized clinical trials and 21 non-randomized controlled studies indicates a reduction of need for target-vessel revascularization with similar outcomes regarding stent thrombosis, myocardial infarction and mortality.
However, this analysis is based on sparse intermediate term data and more long-term data is needed to support use of DES in saphenous vein grafts.

**Background**

Coronary artery bypass graft (CABG) is among the most frequently performed surgical procedures in the U.S. and Europe and a mainstay of therapy for coronary artery disease (CAD). Saphenous vein grafts are the most common type of the grafts used in coronary by-pass surgery. SVG interventions currently account for approximately 10% of total PCI procedures annually in the United States.(1) This number is likely to increase in the near future since there is emerging evidence that even lower degree stenoses (30-60%) may profit from stent implantations;(2) very much in contrast to stenoses in native vessels where increasing data suggest that only hemodynamically significant higher degree stenoses should be treated.(3) The natural and post-interventional biological behaviour of saphenous vein grafts clearly differs from native vessels, they are at higher risk for restenosis.(4) While BMS are currently the gold standard for SVG stenosis, the off-label use of DES has shown promising results in several observational studies while there is a dearth of adequately powered randomized trials. (5-7) These trials have produced conflicting results but each trial lacks sufficient statistical power to detect a difference in clinical endpoints
The aim of this meta-analysis was to review and analyze the current literature for controlled randomized and non-randomized studies comparing drug-eluting stents (DES) versus bare-metal stents (BMS) for treatment of SVG stenoses.

**Methods**

*Eligibility criteria*

Planning and study design was done by two authors (HSG, PM) including creation of an electronic database with variables of interest (Microsoft Excel). Primary and secondary

endpoints, variables of interest and search strategy (databases, sources for unpublished data) were defined in a strategy outline which can be obtained from study authors on request.

We included controlled (randomized and non-randomized) studies that compared DES and BMS (with and without the use of protection devices) in patients with saphenous vein graft (SVG) stenosis. The outcome of primary interest was TVR and the secondary outcomes were myocardial infarction, stent thrombosis or death. Because we expected paucity of data, observational studies were not excluded *a-priori* even though the primary focus was on RCT.

We searched EMBASE, PubMed, MEDLINE, the Cochrane Central Register of Controlled Trials, International Pharmaceutical Abstracts database, ISI Web of Science, and google scholar from 2002 through February 11, 2010. In addition, abstract lists and conference proceedings from the 2006 to 2009 scientific meetings of the American College of Cardiology, and the 2006 to 2009 meetings of the European Society of Cardiology, the Transcatheter Cardiovascular Therapeutics, and the American Heart Association were included. We also considered published review articles, editorials, and internet-based sources of information (www.tctmd.com, www.theheart.org) to assess potential information on studies of interest..

Search strategy for MEDLINE was: **"**saphenous vein graft**"** [All Fields] AND (**"**bare-metal stent**"** [All Fields] OR **"**drug-eluting stent**"** [All Fields] OR **"**paclitaxel-eluting stent"[All Fields] OR **"**sirolimus-eluting stent**"** "[All Fields] OR **"**everolimus-eluting stent**"** [All Fields] OR zatarolimus-eluting stent" [All Fields] OR "stents**"** [MeSH Terms] ). "No restriction on subheadings was applied. Similar but adapted search terms were used for the other literature databases.

Reference lists of selected articles were reviewed for other potentially relevant citations. Authors of selected studies were contacted to obtain further information. All trials comparing DES versus BMS in patients with SVG were included in this analysis.

*Study selection*

In a two-step selection process, two investigators (HSG and PM) independently reviewed the titles and abstracts of all citations to identify all potentially relevant studies. In a second step the corresponding publications were reviewed in full text by the same two investigators to assess if studies were meeting the following inclusion criteria: direct comparison of DES vs. BMS, controlled trial including a BMS control group, and reporting clinical outcomes (TVR, death, ST or MI; Figure 1). Reviewers were not blinded to study authors or outcomes. Final inclusion of studies was based on agreement of both reviewers.

*Data extraction*

The relevant information from the articles including baseline clinical characteristics of the study population was extracted by two investigators (PM and UT).

*Data synthesis and analysis*

All analyses were performed on an intention-to-treat basis. Continuity correction was used when an event did not occur in one group.(8)We evaluated the presence of heterogeneity across trials with the Q and $I^2$ statistics, an $I^2$ value >25% was regarded as relevant heterogeneity. Observational studies and RCT were combined separately and pooled odds ratios (OR) of effect sizes for DES compared with BMS were estimated using a fixed-effects model with Mantel-Haenszel weights in case of low between study heterogeneity or random-effect models with the DerSimonian-Laird approach in case of relevant study heterogeneity

($I^2$ >25%). Data are presented as OR point estimate with 95% confidence intervals within brackets.

Weighted meta-analytical prevalence estimates for outcome in DES and BMS patients were calculated using the variance stabilising Freeman-Tukey double arcsine transformation with an inverse variance random effects model.(9)All analyses were performed with R version 2.9.0(10) (packages "meta", "metafor" and "rmeta") and SAS, version 9.2 (SAS Institute, Cary, NC) (proc mixed).(11)

**Results**

A total of 196 articles were reviewed, and 24 studies including 6391 patients (202 in RCT) satisfied the predetermined strict inclusion criteria; among these, 3 were RCT (Figure 1). (5-7,12) Table 1 summarizes the characteristics of the studies. The other 21 studies were observational .(13-32)

*Primary endpoint*

TVR: In the 3 RCT, TVR occurred in 22.3% [12.1 – 34.7%] of patients with DES and in 36.3% [26.9-46.4%] of patients with BMS. The summary OR was 0.51 [0.27 - 0.96]; p=0.037; heterogeneity $I^2$=16.2%; p=0.303; Figure 2) in favor of DES.

The OR for the observational studies was 0.64 [0.48 - 0.85]; p=0.002; heterogeneity: $I^2$=61.4 %, p=0.0001).

*Secondary endpoints*

Myocardial infarction: In the 3 RCT, infarction occurred in 13.7% [7.0 – 21.7%] of patients after DES implantation compared to 11.1% [0.5 – 33.1%] after BMS implantation. The OR for RCT exclusively was 1.25 [0.22 - 6.99]; p=0.250; heterogeneity: $I^2$=64.8%; p=0.058) (Figure 3). In the observation studies, the OR was found to be 0.75 [0.53 - 1.06]; p= 0.107; heterogeneity: $I^2$= 32.8%; p=0.106).

Stent thrombosis: In the 2 RCT reporting on this endpoint, the OR for DES compared to BMS was 0.78 (0.03 - 21.73, p=0.885; heterogeneity: $I^2$= 68.2%; p=0.076) (Figure 4). The OR for the observational studies was in favor of DES (0.49 [0.25 - 0.94]; p=0.0324 ; heterogeneity: $I^2$= 0%; p=0.794).

Mortality: For the 3 RCT, the OR for mortality between DES and BMS was 2.2 (0.17 – 29.5; p=0.546; heterogeneity: $I^2$=75.8%;p=0.019). For the observational studies, the OR for mortality for DES compared to BMS was 0.66 [0.54 - 0.81]; p < 0.0001; heterogeneity: $I^2$=0%; p=0.641] (Figure 5).

**Discussion**

In this meta-analysis of 24 studies (3 RCT and 21 observational studies) including 6408 patients, DES were superior to BMS with regard to TVR while no difference was found in risk for stent infarction or stent thrombosis in the RCT. The observational studies revealed a reduced risk for stent thrombosis and mortality risk for DES but these finding may be explained by selection bias.

Saphenous vein graft stenting is an entity that has to be investigated specifically. SVG are different in many regards from arterial vessels. Media layers of the SVG are thinner than that of coronary arteries, and thus, is likely to be more susceptible to the mechanical damage caused by stents and balloon pressure. Media fracture has been associated with exaggerated neointimal response.(33) Usually, degenerated vein grafts stenoses are due to soft friable plaques without fibrous cap. Classical atherogenesis probably plays a minor role, hypothesized mechanisms are intimal thrombus that convents into fibrous plaque, change in wall stress (“arterialization” of the vein) and impairment of intrinsic vascular supply.(34,35)

Although restenosis rates are markedly higher in SVG compared with native vessels, classically, BMS is the treatment of choice for SVG stenoses(7) while this setting is regarded an off-label use for DES. However, DES are commonly used in various clinical settings to treat native coronary artery lesions and have been shown to reduce restenosis rates, especially in patients with higher risk for restenosis (diabetes mellitus, small vessels etc.). Saphenous vein graft stenting clearly represents a higher risk setting. Thus, DES are nowadays increasingly being used off-label to treat SVG stenoses, there are limited safety and efficacy data available in this setting. On the other hand, there have been even increased concerns and data suggesting that the effect of DES may be attenuated by the different biological properties of vein grafts or that DES may even be harmful.(12,33)

While short term results from the RRISC trial appeared promising with late lumen loss, restenosis rates, and TVR significantly reduced at 6 months in patients treated with sirolimus-eluting stents (SES), longer term results showed that patients with SES had higher mortality rates than their BMS counterparts and similar rates of TVR. (5,12). Recent observational data suggested also a late “catch-up” phenomenon regarding TVR with a clear benefit for DES in the first year but similar longer term results.(36) It seems plausible that, after the coating drug has completely eluted, the beneficial effect of DES compared to BMS decreases. Due to the different biological properties of saphenous vein grafts, this late “catch up” phenomenon may be more pronounced than in native vessels.

*Limitations*

The main limitation of this study is the small number of RCT available for inclusion. Furthermore, each of the 3 RCT was rather small. (5-7) The meta-analysis of the

observational studies are reflecting the “real-world” and further support the conclusion but observational data are of course prone to bias toward patient selection. (16)

We have to acknowledge that even our pooled analysis is very limited in statistical power and the results showed only a borderline significance for TVR. On the other hand, the observational studies in this meta-analysis support that DES may be beneficial regarding TVR in SVG. Observational data are, of course, prone to bias due to non-random treatment allocation.

Further, it must be noted that a majority of the studies had a short follow-up period (6-12 months). It has also to be considered that two of the three included RCT, the RRISC and the SOS trial, used an angiographic primary endpoint. Better angiographic outcomes do not necessarily translate to better clinical outcomes and angiographic follow-up does not reflect the “real-world”. Thus, these two trials may overestimate the need for repeat TVR.

**Conclusion**

Our meta-analysis suggests that the use of DES is superior to the use BMS for treatment of SVG with regard to TVR but that there are no differences in safety endpoints such as infarction, stent thrombosis or infarction risk.

**Competing interests**

Dr. Meier is supported by the Swiss National Foundation and the “Schweizerische Stiftung für Medizinisch-Biologische Forschung (SSMBS foundation) . We have no competing interests to declare.

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**Figure Legends**

**Figure 1** Flow chart depicting outline of the search and selection strategy

DES=drug-eluting stent; BMS=bare metal stent; SVG=saphenous vein graft.

**Figure 2** The Forest plot of odds ratios (OR) of target-vessel revascularization (TVR). Sizes of data markers are proportional to the weight of each study in the meta-analysis. Horizontal bars, 95% CI. Observational=observational, non-randomized controlled studies; DES=drug-eluting stent; BMS=bare metal stent; RCT=randomized controlled trials.

**Figure 3** The Forest plot of odds ratios (OR) of myocardial infarction. Sizes of data markers are proportional to the weight of each study in the meta-analysis. Horizontal bars, 95% CI. Observational=observational, non-randomized controlled studies; DES=drug-eluting stent; BMS=bare metal stent; RCT=randomized controlled trials.

**Figure 4** The Forest plot of odds ratios (OR) of stent thrombosis (ST), stratified by study type. Sizes of data markers are proportional to the weight of each study in the meta-analysis. Horizontal bars, 95% CI. Observational=observational, non-randomized controlled studies; DES=drug-eluting stent; BMS=bare metal stent; RCT=randomized controlled trials.

**Figure 5** The Forest plot of odds ratios (OR) of mortality, stratified by study type. Sizes of data markers are proportional to the weight of each study in the meta-analysis. Horizontal bars, 95% CI. Observational=observational, non-randomized controlled studies; DES=drug-eluting stent; BMS=bare metal stent; RCT=randomized controlled trials

Table 1: Characteristics of included studies

| Study | N | Stent | Follow up (mts) | Remarks | Patient age (yrs) | Graft age (yrs) | Protection device (%) |
|---|---|---|---|---|---|---|---|
| **Randomized controlled trials** | | | | | | | |
| BASKET | 13 | BMS | 18 | | 71 | na | na |
| | 34 | DES | 18 | SES and PES | 71 | na | na |
| Delayed RRISC | 37 | BMS | median 32 | | 72 | 12.6 | na |
| | 38 | DES | median 30.5 | SES | 73 | 12.4 | na |
| SOS | 39 | BMS | median 18 | | 67 | 12.0 | 56 |
| | 41 | DES | median 18 | PES | 66 | 11.0 | 51 |
| **Observational studies** | | | | | | | |
| Ge et al. | 89 | BMS | 6 | na | 67 | 9.2 | 22.5 |
| | 61 | DES | | na | 67 | 9.7 | 31.1 |
| Lee et al. | 84 | BMS | mean 9 | | 69 | na | 15 |
| | 139 | DES | mean 10 | 211 SES; 78 PES | 69 | na | 19 |
| Chu et al. | 57 | BMS | 12 | | 71 | 9.4 | 100 |
| | 48 | DES | 12 | SES | 69 | 10.1 | 100 |
| Hoffman et al. | 60 | BMS | 6 (TLR) | | 67 | na | 52 |
| | 60 | DES | 6 (TLR) | PES | 67 | na | 64 |
| Wohrle et al. | 26 | BMS | 12 | | 70 | 9.1 | 0 |
| | 13 | DES | 12 | PES | 71 | 11.4 | 0 |
| Ellis et al. | 175 | BMS | 12 | | 69 | 9.8 | 25.1 |
| | 175 | DES | 12 | SES | 70 | 10.0 | 35.6 |
| Minutello et al. | 50 | BMS | mean 20 | | 69 | na | 48 |
| | 59 | DES | mean 21 | SES | 71 | na | 71.2 |
| Bansal et al. | 72 | BMS | mean 33 | | 65 | na | 27 |
| | 37 | DES | mean 34 | 95% SES; 5% PES | 68 | na | 39 |
| Gioia et al. | 119 | BMS | up to 23 | | 70 | 11.0 | na |
| | 106 | DES | up to 23 | 106 SES; 48 PES | 71 | 11.0 | na |
| Assali et al. | 43 | BMS | 24 | | 71 | 11.4 | 48 |
| | 68 | DES | 24 | SES | 70 | 10.8 | 38 |
| van Twisk et al. | 128 | BMS | 48 | | 69 | na | na |
| | 122 | DES | 48 | SES, PES | 68 | | na |
| Vignali et al. | 288 | BMS | median 13.7 | | 71 | 10.7 | na |
| | 72 | DES | median 13.8 | na | 75 | 9.0 | na |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Wilson et al. | 281 | BMS | 9 | | na | na | na |
| | 418 | DES | 9 | 243 SES, 171 PES | na | na | na |
| May et al. | 176 | BMS | 12 (TLR) | | 69 | na | na |
| | 201 | DES | 13 (TLR) | na | 69 | na | na |
| Voudris et al. | 40 | BMS | mean 22.5 | | na | na | na |
| | 43 | DES | mean 22.6 | 90 % SES; 10% PES | na | na | na |
| Moore et al. | 173 | BMS | 12 (TLR) | | 67 | na | na |
| | 171 | DES | 13 (TLR) | SES,PES | 69 | na | na |
| Okabe et al. | 344 | BMS | 12 | | 70 | na | 21 |
| | 138 | DES | 12 | 17 SES; 66 PES | 70 | na | 26 |
| Applegate et al. | 74 | BMS | 24 | | 69 | na | 47 |
| | 74 | DES | 24 | 67 SES; 7 PES | 69 | na | 53 |
| Shishehbor et al.(13) | 349 | BMS | 35 | | 69 | na | 30 |
| | 217 | DES | 35 | na | 70 | na | 56 |
| Lozano et al.(32) | 114 | BMS | 30 | | 71 | 121 | na |
| | 98 | DES | 30 | na | 66 | 108 | na |
| Brodie et al.(36) | 343 | BMS | 9 | | 69 | na | 33.7 |
| | 785 | DES | 9 | 59% SES, 38% PES, 3% both | 68 | na | 37.3 |

BMS: bare-metal stent; DES: drug-eluting stent; na: not available; PES: paclitaxel-eluting stent; SES: sirolimus-eluting stent; TLR: target lesion revascularization; TVR: target vessel revascularization.

**References**


1. Wilson CT, Fisher ES, Welch HG, Siewers AE, Lucas FL. U.S. trends in CABG hospital volume: the effect of adding cardiac surgery programs. Health Aff (Millwood) 2007;26:162-8.
2. Rodes-Cabau J, Bertrand OF, Larose E, et al. Comparison of plaque sealing with paclitaxel-eluting stents versus medical therapy for the treatment of moderate nonsignificant saphenous vein graft lesions: the moderate vein graft lesion stenting with the taxus stent and intravascular ultrasound (VELETI) pilot trial. Circulation 2009;120:1978-86.
3. Tonino PA, De Bruyne B, Pijls NH, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med 2009;360:213-24.
4. Safian RD. Accelerated atherosclerosis in saphenous vein bypass grafts: a spectrum of diffuse plaque instability. Prog Cardiovasc Dis 2002;44:437-48.
5. Vermeersch P, Agostoni P, Verheye S, et al. Randomized double-blind comparison of sirolimus-eluting stent versus bare-metal stent implantation in diseased saphenous vein grafts: six-month angiographic, intravascular ultrasound, and clinical follow-up of the RRISC Trial. J Am Coll Cardiol 2006;48:2423-31.
6. Jeger RV, Schneiter S, Kaiser C, et al. Drug-eluting stents compared with bare metal stents improve late outcome after saphenous vein graft but not after large native vessel interventions. Cardiology 2009;112:49-55.
7. Brilakis ES, Lichtenwalter C, de Lemos JA, et al. A randomized controlled trial of a paclitaxel-eluting stent versus a similar bare-metal stent in saphenous vein graft


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lesions the SOS (Stenting of Saphenous Vein Grafts) trial. J Am Coll Cardiol 2009;53:919-28.

8. Sankey S, Weissfeld L, Fine M, et al. An assessment of the use of the continuity correction for sparse data in metanalysis. Communications in Statistics: Simulation and Computation 1996;25:1031-56.

9. Miller J. The inverse of the Freeman-Tukey double arcsine transformation. The American Statistician 1978;32.

10. Software. RS. R Development Core Team (2009). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org. 2.7.1 ed. Vienna, Austria: R Foundation for Statistical Computing.

11. Hartung J, Knapp G, Sinha BK. Statistical Meta-Analysis with Applications. 1 ed. Hoboken, NJ: Wiley-Interscience, 2008.

12. Vermeersch P, Agostoni P, Verheye S, et al. Increased late mortality after sirolimus-eluting stents versus bare-metal stents in diseased saphenous vein grafts: results from the randomized DELAYED RRISC Trial. J Am Coll Cardiol 2007;50:261-7.

13. Shishehbor MH, Hawi R, Singh IM, et al. Drug-eluting versus bare-metal stents for treating saphenous vein grafts. Am Heart J 2009;158:637-43.

14. Chu WW, Rha SW, Kuchulakanti PK, et al. Efficacy of sirolimus-eluting stents compared with bare metal stents for saphenous vein graft intervention. Am J Cardiol 2006;97:34-7.

15. Ge L, Iakovou I, Sangiorgi GM, et al. Treatment of saphenous vein graft lesions with drug-eluting stents: immediate and midterm outcome. J Am Coll Cardiol 2005;45:989-94.

16. Lee MS, Shah AP, Aragon J, et al. Drug-eluting stenting is superior to bare metal stenting in saphenous vein grafts. Catheter Cardiovasc Interv 2005;66:507-11.

Formatiert: Italienisch (Italien)

17. Hoffmann R, Pohl T, Koster R, Blindt R, Boeckstegers P, Heitzer T. Implantation of paclitaxel-eluting stents in saphenous vein grafts: clinical and angiographic follow-up results from a multicentre study. Heart 2007;93:331-4.

18. Wohrle J, Nusser T, Kestler HA, Kochs M, Hombach V. Comparison of the slow-release polymer-based paclitaxel-eluting Taxus-Express stent with the bare-metal Express stent for saphenous vein graft interventions. Clin Res Cardiol 2007;96:70-6.

19. Ellis SG, Kandzari D, Kereiakes DJ, et al. Utility of sirolimus-eluting Cypher stents to reduce 12-month target vessel revascularization in saphenous vein graft stenoses: results of a multicenter 350-patient case-control study. J Invasive Cardiol 2007;19:404-9.

20. Minutello RM, Bhagan S, Sharma A, et al. Long-term clinical benefit of sirolimus-eluting stents compared to bare metal stents in the treatment of saphenous vein graft disease. J Interv Cardiol 2007;20:458-65.

21. Wilson BH, Humphrey AD, Cedarholm JC, et al. Drug-eluting stents are no better than bare metal stents in vein grafts: results from the strategic transcatheter evaluation of new therapies (STEMT) group (abstract). American College of Cardiology ACC and SCAI Summit meeting. Chicago, IL, 2007.

22. Voudris V, Kalianos C, Patsilinakos S, et al. Effectiveness of drug-eluting stents in the treatment of bypass graft lesions (abstract). Eur Heart J 2006, 27(Abstract Suppl), 925.

23. Moore PA, Toney BM, Hermiller JB. Off label use of drug-eluting stents: no advantage in saphenous vein grafts. Transcatheter Cardiovascular Therapheutics (TCT), 2007.

24. Bansal D, Muppidi R, Singla S, et al. Percutaneous intervention on the saphenous vein bypass grafts--long-term outcomes. Catheter Cardiovasc Interv 2008;71:58-61.

Formatiert: Französisch (Frankreich)

25. Gioia G, Benassi A, Mohendra R, Chowdhury K, Masood I, Matthai W. Lack of clinical long-term benefit with the use of a drug eluting stent compared to use of a bare metal stent in saphenous vein grafts. Catheter Cardiovasc Interv 2008;72:13-20.

26. Assali A, Raz Y, Vaknin-Assa H, et al. Beneficial 2-years results of drug-eluting stents in saphenous vein graft lesions. EuroIntervention 2008;4:108-14.

27. van Twisk PH, Daemen J, Kukreja N, van Domburg RT, Serruys PW. Four-year safety and efficacy of the unrestricted use of sirolimus- and paclitaxel-eluting stents in coronary artery bypass grafts. EuroIntervention 2008;4:311-7.

28. Vignali L, Saia F, Manari A, et al. Long-term outcomes with drug-eluting stents versus bare metal stents in the treatment of saphenous vein graft disease (results from the REgistro Regionale AngiopLastiche Emilia-Romagna registry). Am J Cardiol 2008;101:947-52.

29. May HT, Bair TL, Muhlestein JB, et al. **Use of Drug-Eluting Stents in Saphenous Vein Graft Lesions (abstract)** Journal of the American College of Cardiology, March 11, 2008, Volume 51, Issue 10, Supplement A.

30. Okabe T, Lindsay J, Buch AN, et al. Drug-eluting stents versus bare metal stents for narrowing in saphenous vein grafts. Am J Cardiol 2008;102:530-4.

31. Applegate RJ, Sacrinty M, Kutcher M, Santos R, Gandhi S, Little W. Late outcomes of drug-eluting versus bare metal stents in saphenous vein grafts: Propensity score analysis. Catheter Cardiovasc Interv 2008;72:7-12.

32. Lozano I, Garcia-Camarero T, Carrillo P, et al. [Comparison of drug-eluting and bare metal stents in saphenous vein grafts. Immediate and long-term results]. Rev Esp Cardiol 2009;62:39-47.

33. Ribichini F, Pugno F, Ferrero V, et al. Long-term histological and immunohistochemical findings in human venous aorto-coronary bypass grafts. Clin Sci (Lond) 2008;114:211-20.

34. Brody WR, Kosek JC, Angell WW. Changes in vein grafts following aorto-coronary bypass induced by pressure and ischemia. J Thorac Cardiovasc Surg 1972;64:847-54.

35. Bulkley BH, Hutchins GM. Accelerated "atherosclerosis". A morphologic study of 97 saphenous vein coronary artery bypass grafts. Circulation 1977;55:163-9.

36. Brodie BR, Wilson H, Stuckey T, et al. Outcomes with drug-eluting versus bare-metal stents in saphenous vein graft intervention results from the STENT (strategic transcatheter evaluation of new therapies) group. JACC Cardiovasc Interv 2009;2:1105-12.